

CLAIM AMENDMENTS:

Claims 1, 12, 15, 18, 19, 21, 30, 33, 36 and 37 have been amended, and new dependent claims 39-44 have been added. No new matter is believed to have been added by these changes. The following listing of claims will replace all prior versions and listings, of claims in this Application:

Listing of Claims:

Claim 1 (Currently Amended): A formulated liposome for incorporating high content of hydrophobic substances comprising:

a first phospholipid, selected from a hydrogenated naturally-occurring phospholipid or a saturated phospholipid with long carbon chains $-(CH_2)_n-$, the value of n is at least 14);

a second phospholipid, selected from an unsaturated phospholipid or a saturated phospholipid with short carbon chains $-(CH_2)_n-$, the value of n is at most 14) ;

one or more hydrophobic substances; and

liposome-forming materials,

wherein the first and the second phospholipid coexist in the liposome in two immiscible phases and create several discontinuous regions, and a molar ratio of the first phospholipid to the second phospholipid is larger no less than ~~4/20~~ 3/16; a phase transition temperature T_{g1} of the first phospholipid is in the range between 40 and 74 °C, and a phase transition temperature T_{g2} of the second phospholipid is in the range between -30 and 10 °C while a drug delivery temperature T_1 and a drug storage temperature T_2 are chosen at specified ranges subject to an order of $T_{g1} > T_1 > T_2 > T_{g2}$.

Claim 2 (Original): The liposome according to claim 1, wherein the phase transition temperature of the first phospholipid is preferably in the range between 50 and 65 °C, and the phase transition temperature of the second phospholipid is preferably in the range between -20 and 4 °C.

Claim 3 (Original): The liposome according to claim 1, wherein the first phospholipid is selected from the group consisting of phosphatidyl choline (PC), phosphatidyl glycerol (PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

Claim 4 (Previously Presented): The liposome according to claim 3, wherein phospholipid is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearyl phosphatidyl choline (DSPC), diarachidoyl phosphatidyl choline, dimyristoyl phosphatidyl ethanolamine (DMPE), dipalmitoyl phosphatidyl ethanolamine (DPPE), distearoyl phosphatidyl ethanolamine (DSPE), dipalmitoyl phosphatidyl glycerol (DPPG), distearoyl phosphatidyl glycerol, dimyristoyl phosphatidyl acid (DMPA), dipalmitoyl phosphatidyl acid (DPPA), dipalmitoyl phosphatidyl serine (DPPS), and distearoyl phosphatidyl serine (DSPS).

Claim 5 (Original): The liposome according to claim 1, wherein the second phospholipid is selected from the group consisting of phosphatidyl choline (PC), phosphatidyl glycerol (PG), phosphatidyl serine (PS), phosphatidyl acid (PA) and phosphatidyl ethanolamine (PE).

Claim 6 (Previously Presented): The liposome according to claim 5, wherein phospholipid is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, dipetroselinoyl phosphatidyl choline, dipalmitelaidoyl phosphatidyl choline, dioleoyl phosphatidyl ethanolamine, dioleoyl phosphatidyl serine, dilauroyl phosphatidyl choline (DLPC), diundecanoyl phosphatidyl choline, didecanoyl phosphatidyl ethanolamine, and dinonanoyl phosphatidyl ethanolamine.

Claim 7 (Original): The liposome according to claim 1, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

Claim 8 (Previously Presented): The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is paclitaxel and/or docetaxel.

Claim 9 (Previously Presented): The liposome according to claim 8, wherein paclitaxel and/or docetaxel are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 25 mole%.

Claim 10 (Previously Presented): The liposome according to claim 9, wherein paclitaxel and/or docetaxel are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 11 (Previously Presented): The liposome according to claim 9, wherein paclitaxel and/or docetaxel are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 12 (Currently Amended): The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is retinoic acid and/or a derivative thereof, the retinoic acid ~~derivatives~~ derivative is selected from the group consisting of include retinol, retinyl acylate and retinyl acetate.

Claim 13 (Original): The liposome according to claim 12, wherein the retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 40 mole%.

Claim 14 (Original): The liposome according to claim 13, wherein retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 10 mole% to 40 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 15 (Currently Amended): The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is camptothecin and/or a derivative thereof, wherein the ~~derivatives~~ derivative of camptothecin is selected from the group consisting of ~~include~~ irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

Claim 16 (Original): The liposome according to claim 15, wherein the camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 30 mole%.

Claim 17 (Original): The liposome according to claim 16, wherein camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 18 (Currently Amended): The liposome according to claim 7, wherein the hydrophobic pharmaceutical compound is selected from the group consisting of paclitaxel and/or a paclitaxel derivative ~~derivatives thereof~~, retinoic acid and/or a retinoic acid derivative ~~the derivatives thereof~~, and camptothecin and/or a camptothecin derivative ~~the derivatives thereof~~, wherein the derivative of paclitaxel includes ~~is~~ docetaxel; the ~~derivatives of~~ retinoic acid derivative include ~~is selected from the group consisting of~~ retinol, retinyl acylate and retinyl acetate; the ~~derivatives of~~ camptothecin derivative ~~include~~ is selected from the group consisting of irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-

methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

Claim 19 (Currently Amended): The liposome according to claim 1, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, cholesterol derivatives, antioxidant, and mixtures thereof, wherein cholesterol derivatives are selected from the group consisting of ~~include~~ polyethylene glycol 600 mono(cholesteryl) ether sebacate and cholesteryl oleyl carbonate.

Claim 20 (Original): The liposome according to claim 19, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearoyl phosphatidyl ethanolamine (MPEG-DSPE).

Claim 21 (Currently Amended): A liposome for incorporating high content of hydrophobic substances comprising:

a first phosphatidyl choline, selected from a hydrogenated naturally-occurring phospholipid or a saturated phospholipid with long carbon chains ($-(CH_2)_n-$, the value of n is at least 14);

a second phosphatidyl choline, selected from an unsaturated phospholipid or a saturated phospholipid with short carbon chains ($-(CH_2)_n-$, the value of n is at most 14); one or more hydrophobic substances; and

liposome-forming materials,

wherein the first and the second phosphatidyl cholines coexist in the liposome in two immiscible phases and create several discontinuous regions, and a molar ratio of the first phosphatidyl choline to the second phosphatidyl choline is ~~larger~~ no less than 4/20 3/16; a phase transition temperature T_{g1} of the first phosphatidyl choline is in the range between 40 and 74°C, and a phase transition temperature T_{g2} of the second phosphatidyl choline is in the range between -30 and 10°C, and a drug delivery temperature T_1 and a drug storage temperature T_2 are chosen at specified ranges subject to an order of $T_{g1} > T_1 > T_2 > T_{g2}$.

Claim 22 (Original): The liposome according to claim 21, wherein the phase transition temperature of the first phospholipid is preferably in the range from 50 to 65°C, and the phase transition temperature of the second phospholipid is preferably in the range from -20 to 4°C.

Claim 23 (Original): The liposome according to claim 21, wherein the first phosphatidyl choline (PC) is selected from the group consisting of hydrogenated egg phosphatidyl choline (HEPC), hydrogenated soy phosphatidyl choline (HSPC), dipalmitoyl phosphatidyl choline (DPPC) and distearyloyl phosphatidyl choline (DSPC),

Claim 24 (Previously Presented): The liposome according to claim 21, wherein the second phosphatidyl choline is selected from the group consisting of egg phosphatidyl choline (EPC), soy phosphatidyl choline (SPC), synthetic or natural-occurring unsaturated phosphatidyl cholines and dilauroyl phosphatidyl choline (DLPC), oleoyl palmitoyl phosphatidyl choline, dioleoyl phosphatidyl choline, and dipetroselinoyl phosphatidyl choline, dipalmitelaidoyl phosphatidyl choline.

Claim 25 (Original): The liposome according to claim 21, wherein the hydrophobic substances are one or more hydrophobic pharmaceutical compounds.

Claim 26 (Previously Presented): The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is paclitaxel and/or docetaxel.

Claim 27 (Previously Presented): The liposome according to claim 26, wherein the paclitaxel and/or docetaxel are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 25 mole%.

Claim 28 (Previously Presented): The liposome according to claim 27, wherein paclitaxel and/or docetaxel are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 29 (Previously Presented): The liposome according to claim 27, wherein paclitaxel and/or docetaxel are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 25 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 30 (Currently Amended): The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is retinoic acid and/or a derivative thereof, the retinoic acid ~~derivatives~~ derivative is selected from the group consisting of include retinol, retinyl acylate and retinyl acetate.

Claim 31 (Original): The liposome according to claim 30, wherein the retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 40 mole%.

Claim 32 (Original): The liposome according to claim 31, wherein retinoic acid and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 10 mole% to 40 mole% when the first phospholipid is hydrogenated soy phosphatidyl choline (HSPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 33 (Currently Amended): The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is camptothecin and/or a derivative, and the ~~derivatives~~ derivative of camptothecin is selected from the group consisting of include irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

Claim 34 (Original): The liposome according to claim 33, wherein the camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 0.5 mole% to 30 mole%.

Claim 35 (Original): The liposome according to claim 34, wherein camptothecin and/or the derivative thereof are/is incorporated with a drug/lipid ratio ranging from about 5 mole% to 30 mole% when the first phospholipid is hydrogenated egg phosphatidyl choline (HEPC) and the second phospholipid is egg phosphatidyl choline (EPC).

Claim 36 (Currently Amended): The liposome according to claim 25, wherein the hydrophobic pharmaceutical compound is selected from the group consisting of paclitaxel, retinoic acid, camptothecin and the derivatives thereof, wherein the derivative of paclitaxel ~~includes~~ is docetaxel; the derivatives of retinoic acid are selected from the group consisting of ~~include~~ retinol, retinyl acylate and retinyl acetate; the derivatives of camptothecin are selected from the group consisting of ~~include~~ irinotecan, topotecan, SN-38, 9-aminocamptothecin, 7-ethylcamptothecin, 10-hydroxycamptothecin, 9-nitrocamptothecin, 10,11-methylenedioxycamptothecin, 9-amino-10,11-methylenedioxycamptothecin, 9-chloro-10,11-methylenedioxycamptothecin, 7-(4-methylpiperazinomethylene)-10,11-ethylenedioxy-20(S)-camptothecin, 7-(4-methylpiperazinomethylene)-10,11-methylenedioxy-20(S)-camptothecin and 7-(2-N-isopropylamino)ethyl)-(20S)-camptothecin.

Claim 37 (Currently Amended): The liposome according to claim 21, wherein the liposome-forming materials are selected from the group consisting of hydrophilic polymer-modified lipids, cholesterol, cholesterol derivatives, antioxidant, and mixture thereof, wherein cholesterol derivatives are selected from the group consisting of ~~include~~ polyethylene glycol 600 mono(cholesteryl) ether sebacate and cholesteryl oleyl carbonate.

Claim 38 (Original): The liposome according to claim 37, wherein the hydrophilic polymer-modified lipid is methoxy polyethylene glycol-distearoyl phosphatidyl ethanolamine (MPEG-DSPE).

Claim 39 (Newly Added): The liposome according to claim 1, wherein the hydrophobic substance incorporated in the liposome is present in an amount of ranging from about 3 mole% to about 25 mole%.

Claim 40 (Newly Added): The liposome according to claim 1, wherein the hydrophobic substance incorporated in the liposome is present in an amount ranging from about 8 mole% to about 25 mole%, and the liposome remains at at least 70% of incorporation efficiency for at least 60 days.

Claim 41 (Newly Added): The liposome according to claim 1, wherein at least 20 mole% of the hydrophobic substance is incorporated in the liposome and the liposome remains at at least about 70% of incorporation efficiency at the sixth month.

Claim 42 (Newly Added): The liposome according to claim 21, wherein the hydrophobic substance incorporated in the liposome is present in an amount ranging from about 3 mole% to about 25 mole%.

Claim 43 (Newly Added): The liposome according to claim 21, wherein the hydrophobic substance incorporated in the liposome is present in an amount ranging from about 8 mole% to about 25 mole%, and the liposome remains at at least 70% of incorporation efficiency for at least 60 days.

Claim 44 (Newly Added): The liposome according to claim 21, wherein at least 20 mole% of the hydrophobic substance is incorporated in the liposome and the liposome remains at at least about 70% of incorporation efficiency at the sixth month.